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A FURTHER STUDY OF THE PROGNOSTIC VALUE OF ARNETH'S LEUKOCYTIC BLOOD PICTURE IN PUL- MONARY TUBERCULOSIS, BASED UPON 729 COUNTS IN 475 PATIENTS.¹

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THREE years ago, in a paper by Dr. C. L. Minor and myself,² there were reported the results of the first 100 Arneth counts done by us together with deductions as to their probable prognostic value in cases of pulmonary tuberculosis. At this time it is unnecessary to go into the theory of the causation of this blood picture and its variations. Suffice it to say that the blood picture consists in a differential count of the polymorphonuclear neutrophils with respect to the number of their nuclei. Five classes are recognized according to the number of nuclei in this variety of leukocyte. Arneth claims that in cases with low resisting power there is a preponderance of cells with one or two nuclei, while in cases with good resisting power the percentage of leukocytes with three, four, and five nuclei is increased. Thus in bad cases he obtains what he terms a shifting of the blood picture to the left—"Verschiebung nach Links." This blood picture has been studied and Arneth's conclusions substantiated by many workers, including Arloing and Genty, Bushnell and Treuholtz, Edson, Klebs, Webb

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and Williams. The work of Dr. Minor and myself agreed in the main with the results obtained by those mentioned above. We elected to divide our cases according to the clinical symptoms rather than according to the amount of lung involvement, and grouped them into four classes: (1) Good, (2) medium, (3) bad, (4) very bad. Upon going over our counts and making a graphic representation of the results, we found that the one and two nuclei cells were greatest in the classes named "bad" and "very bad," and decreased in the classes named "good" and "medium," while the opposite was true of the cells with three, four, and five nuclei. In a small number of cases—not over 4 or 5—we found together with a good clinical symptom complex a very bad blood picture, and we noted that shortly thereafter the patient took a turn for the worse.

Neither in the counts forming the basis for the paper above referred to, nor in the counts following it, have the polymorphonuclear leukocytes been divided into sub-classes (as Arneth was wont to do) based upon the shape of the nuclei—whether indented, S-shaped, crescentic, etc. This has been deemed unimportant. The same arbitrary rules for counting that were advocated in the article written three years ago have been strictly adhered to. These are: (1) Nuclei connected by an isthmus counted as one nucleus. (By "isthmus" is meant a strand of nuclear matter one-third or more of the thickness of the nucleus.) (2) Nuclei connected by a thread counted as two nuclei. (3) Nuclei clearly superimposed counted as two nuclei. (4) Nuclei tangent to one another counted as two nuclei. Thus uniformity of counts done by the same worker was assured.

So much for a very brief review of the former results published by Dr. Minor and myself. Since that time the use of Arneth counts has been continued, and the writer wishes in this article to set forth conclusions arrived at from a total of 729 counts done on 475 patients. In addition to the counts done on tuberculous or supposedly tuberculous patients, the blood of 20 apparently normal individuals has been counted, in order to arrive at a "normal" blood picture.

The average of these 20 counts gives as a normal blood picture the following:

	I	II	III	IV	V	Index
Percentage	4	20.5	58.5	15	2	53.75

This average is slightly better than that obtained by Arneth from the average of 15 supposedly normal individuals. His "normal" blood picture reads as follows:

	I	II	III	IV	V	Index
Percentage	5	35	41	17	2	60.5

The "index," so-called, is one arbitrarily adopted by Bushnell, and is obtained by adding together the percentages of Classes I and II, and half that of Class III, thus showing what percentage of the cells is to the left in the blood picture. This index has the advantage of showing at a glance whether the blood picture is good or bad, but it has the disadvantage that it tends to relegate into the background the relative proportions of the various classes, and especially that it recognizes no difference between Classes I and II, a difference that is not without importance.

As a result of over 700 counts, the conclusions drawn can be neither as unified nor as satisfactory as those derived three years ago from 100 counts; showing that greater familiarity with a method both enhances its value and indicates its limitations. The writer does not wish to be thought to mean that the Arneth blood picture is to be considered as valueless, misleading, or false. Far from it. The blood picture is of a certain value, it should not be abandoned, and it will in certain apparently favorable cases correctly presage an unfortunate outcome, or *vice versa*. The writer, however, must confess that he cannot place as much weight upon its prognostic value as he did three years back.

First and foremost it must be distinctly understood that the Arneth blood picture can in no way be taken to indicate the amount of lung involvement or the stage of the disease. It is simply and solely an index of the resisting power of the patient. Patients with extensive local lesions—usually of the fibroid type—showing but little activity and having a good general state of nutrition will give a relatively good blood picture; while others with but very slight local lesions, but poor nutritional conditions will give a bad picture. As an example of the first class may be cited the blood picture of a man (J. B. McG.) with fibroid phthisis of fifteen years duration—extensive pulmonary involvement, but good general condition:

	I	II	III	IV	V	Index
Percentage	12	45	35	7	1	74.5

This is a relatively good blood picture, especially when contrasted with that of the following patient (McD.) having but suspicious signs of a unilateral basal pleurisy, no cough, no bacilli in the very scanty sputum, but in very poor general condition. His blood picture was as follows:

	I	II	III	IV	V	Index
Percentage	12	42	42	4	0	75

Which is decidedly bad for a patient with such slight evidences of disease.³

³ Since the writing of this paper the patient here referred to reacted violently to 2 mg. of old tuberculin.

Again, improvement in the blood picture or the reverse, indicates a corresponding change in the resisting powers of the patient and that alone. To be sure such changes are usually accompanied by betterment or further extension of physical signs, but there are always patients to be found whose general condition improves markedly while the physical signs remain stationary, just as there are others that begin to go downhill without any detectable change taking place in the local pulmonary condition. It is in such cases that the blood picture is of distinct value. The 3 following cases will illustrate this point:

CASE I.—In a patient running no fever (W. B.), and with slight unilateral apical catarrh, the following relatively bad picture was found:

	I	II	III	IV	V	Index
Percentage	20	45	36	5	0	80

One month later the reading was:

	I	II	III	IV	V	Index
Percentage	38.5	49.5	10.5	1.5	0	93.5

This was soon followed by an acute exacerbation of his disease which shortly ended fatally.

CASE II.—The patient (Col. B.), a man in excellent condition, showed but the faintest signs of pulmonary involvement—granular or rude breathing at the right apex anteriorly and posteriorly. His blood picture on arrival was:

	I	II	III	IV	V	Index
Percentage	3	29	55	12	1	59.5

Seven weeks later, fourteen pounds having been gained, but the physical signs being identically the same, he showed:

	I	II	III	IV	V	Index
Percentage	4	20	56	18	2	52

CASE III.—A man (Rev. M. L. B.) of slender build and excessively nervous temperament, pale, anemic, and generally run down, showed at both apices definite breath changes, but no adventitious sounds. His blood picture on arrival was:

	I	II	III	IV	V	Index
Percentage	36	48	16	0	0	92

This pointed to an unfavorable termination, despite the slight physical signs. Three months later, having gained much in weight and strength, his lungs showed in addition to the modified breath sounds a few fine crackles at one apex anteriorly and posteriorly. The blood picture at this time, however, showed the following:

	I	II	III	IV	V	Index
Percentage	21	42	27	7	0	79.5

A great improvement substantiated by the man's general condition, despite the increase in physical findings.

These 3 cases serve to stress the point that by means of the Arneth blood picture we obtain an index of the general resisting power of the patient, and of that alone.

In mentioning the index used in the blood picture it was stated that it was apt to be misleading by taking the attention away from the percentage of cells in the various classes, and making no differentiation between Classes I and II. The following case well illustrates this point: A patient (F. R. II.) with marked pulmonary and slight laryngeal involvement showed upon arrival the following bad blood picture:

	I	II	III	IV	V	Index
Percentage	31	46	20	1	2	87

Two and a half months later, having made great improvement, his picture was as follows:

	I	II	III	IV	V	Index
Percentage	15	53	27	5	0	81.5

No very striking difference is seen upon looking at the indices, but it must be noted that the cells in Class I are reduced by over 50 per cent., and the cells in Class IV increased 500 per cent., this being significant despite the loss of cells in Class V.

In the writer's opinion a bad blood picture with the percentage in Class I in excess of that in Class II is far worse than one in which the members of Class II are in the majority.

So far attention has been called to counts tending to prove the value of the blood picture in estimating the resisting power of the patient, and consequently in shaping our prognosis. In all fairness the other side of the question must now be taken up, and cases cited in which the blood picture has been misleading.

It is an undeniable fact that in a small number of cases the blood picture has been at absolute variance with the clinical picture, and the subsequent course of the case has in no way accounted or atoned for the anomalous blood findings. It has been quite impossible to estimate exactly the percentage of cases in which this condition has been found, because of the impracticability of eliminating external (and also internal) agencies that could not be foreseen and that had either a salutary or else a deleterious effect upon the patient. In the writer's opinion about 5 per cent. of the cases show a blood picture totally at variance with the clinical picture, and not borne out by subsequent events. This occurs chiefly in cases with good general symptoms and satisfactory local signs. Two examples will suffice:

CASE I.—A patient (R. S.) came to Asheville in March, 1909, with but slight physical signs and in excellent general condition. However, from the character of the onset of the disease and from the quality of the signs, the trouble was suspected to be of an acute nature. Upon arrival the blood picture was as follows:

	I	II	III	IV	V	Index
Percentage	21	53.5	21	2.5	0	87

Two months later, the patient having markedly improved, the picture read:

	I	II	III	IV	V	Index
Percentage	23	47.5	29	0.5	0	85

There was practically no change.

Two months later, the general and local condition having shown still further improvement, the picture remained unchanged, to wit:

	I	II	III	IV	V	Index
Percentage	20	48	32	0	0	84

The patient has been heard from recently, and is now well and in the best possible condition.

CASE II.—Another patient (R. S. R.) came under observation with but very slight unilateral apical catarrh—no temperature—general condition excellent. The blood picture was distinctly at variance with what would be expected. It read:

	I	II	III	IV	V	Index
Percentage	19	52	23	6	0	82.5

The patient has improved, and is in most satisfactory condition, but the last count done reads as follows:

	I	II	III	IV	V	Index
Percentage	17	55	24	3	1	84

This count shows practically no change.

It would be wearisome to give more examples. The 2 cases cited amply illustrate the point.

Solis Cohen and Strickler⁴ have made a careful study of the Arneth blood picture in cases of pulmonary tuberculosis. Their conclusions are here set forth.

"While the average index showed little change, in most of our individual cases the proportion of cells in the first two classes of Arneth seemed to be increased as the patient improved, and in a number of cases to be decreased as the patient grew worse. Of 27 improving patients whose blood was examined more than

⁴ AMER. JOUR. MED. SCI., November, 1911.

once, an increase in cells with one and two nuclei was observed in 22, and a decrease in 4. Among advancing cases there was an increase in 3, a decrease in 4, and no change in 2. Our figures are opposed to those of all other workers."

Such statements from such reliable authorities deserve serious consideration. It is quite impossible for the writer to explain the discrepancy. It would hardly be likely that the majority of Cohen and Strickler's cases were of the type exemplified by the last two examples cited. The only other way for accounting for the contradictory findings is difference in the method of counting the nuclei, for in certainly 50 per cent. of the cells the nuclei are so placed or so connected that a doubt will arise as to which class the particular cell belongs. Were it possible for all workers in this field to agree upon a common set of rules for the estimation of the number of nuclei, and, furthermore, were it possible for different workers to count each other's smears, the real value of the method would be far better shown.

In a masterful paper on this subject which unfortunately came to the writer's notice but recently, Miller and Reed⁵ point out that the nuclei are greatly affected as to their number by the fact of either finger or slide being contaminated with dirt. This is a distinctly valuable point, and also a prolific source of error. It is gratifying to note that such painstaking workers as those just cited, believe that the Arneth blood picture is of real value in prognosis.

In conclusion, the writer would state that in his opinion the Arneth blood picture has a certain definite value in forming a prognosis in pulmonary tuberculosis. It is a corroboratory factor to the general clinical picture, and should never be given much weight in contradiction to the general symptom complex presented by the patient. In a small number of cases it will presage an unfortunate outcome or else will cause us to pause before giving a bad prognosis. In a small number of cases it will remain opposed to all the general indications found in the patient. In the vast majority of cases it will faithfully represent the patient's resisting powers but will not disclose any new features. The Arneth blood picture is to be viewed with conservatism. Few that take it up and study it carefully will ever abandon it entirely, but he that places implicit confidence in its readings and bases his prognostic opinion chiefly thereon, will not infrequently be led into error.

⁵ Archives of Internal Medicine, May 15, 1912.